



Armed Forces College of Medicine AFCM



Gastric Secretion

By

Dr. Wessam Ezzat Morsy

***Ass. Prof. of Physiology, Faculty of
Medicine, ASU.***

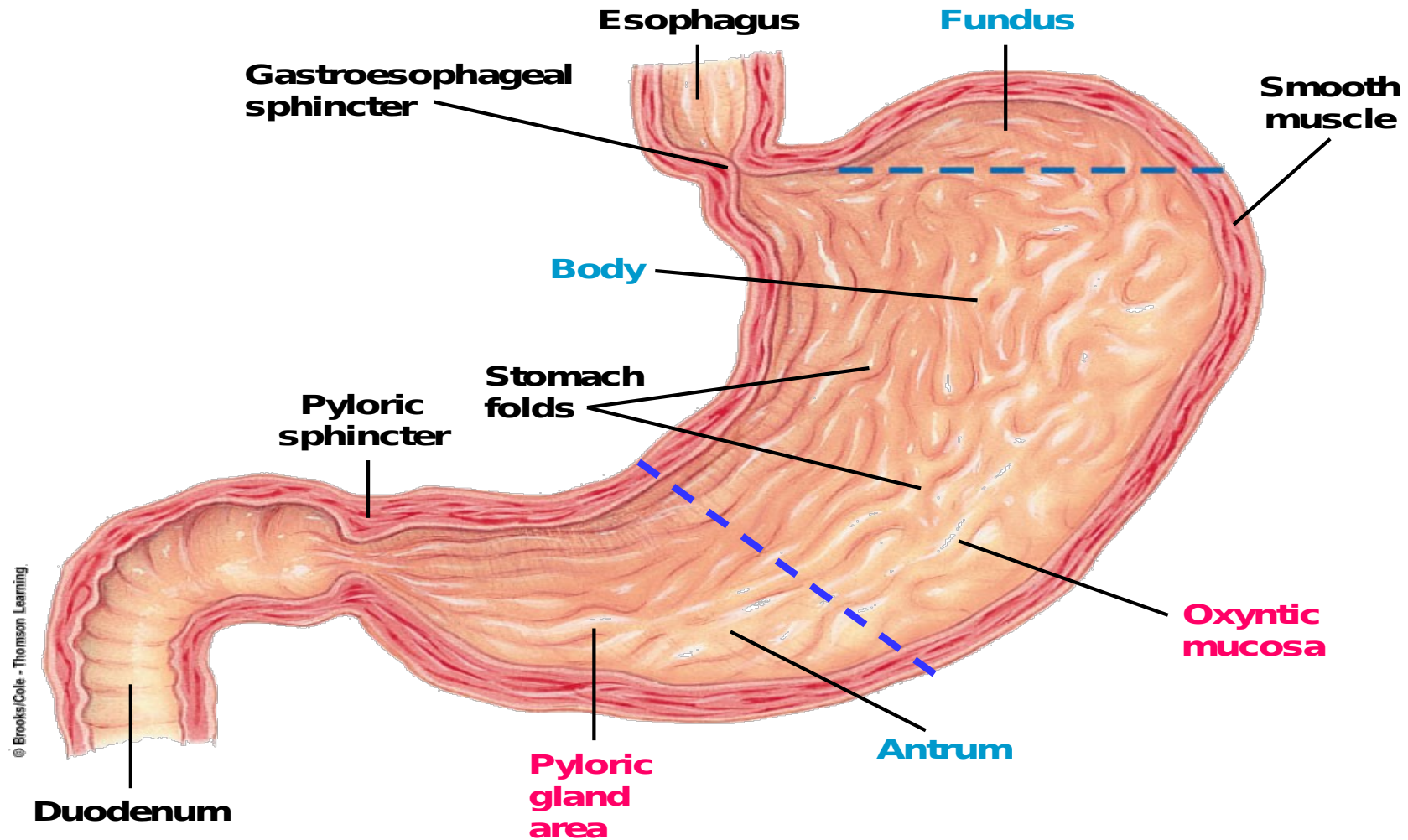
INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture, the student will be able to:

1. Describe the composition of gastric juice and its function.
2. Describe mechanism of HCL formation.
3. Explain the role of gastric HCL in digestion.
4. Discuss regulation of acid secretion of parietal cell.

Gastric Mucosa



Gastric Mucosa

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graph TD; A[Gastric Mucosa] --> B[Oxyntic mucosa]; A --> C[Pyloric gland area];
```

Oxyntic mucosa

Site:

- Fundus
- Body

Contains

- **Parietal** cells □ Hcl, intrinsic factor.
- **Enterochromaffin like** cells □ histamine.
- Mucous **neck** cells □ thin watery mucous
- **Chief** cells □ pepsinogen.

Pyloric gland area

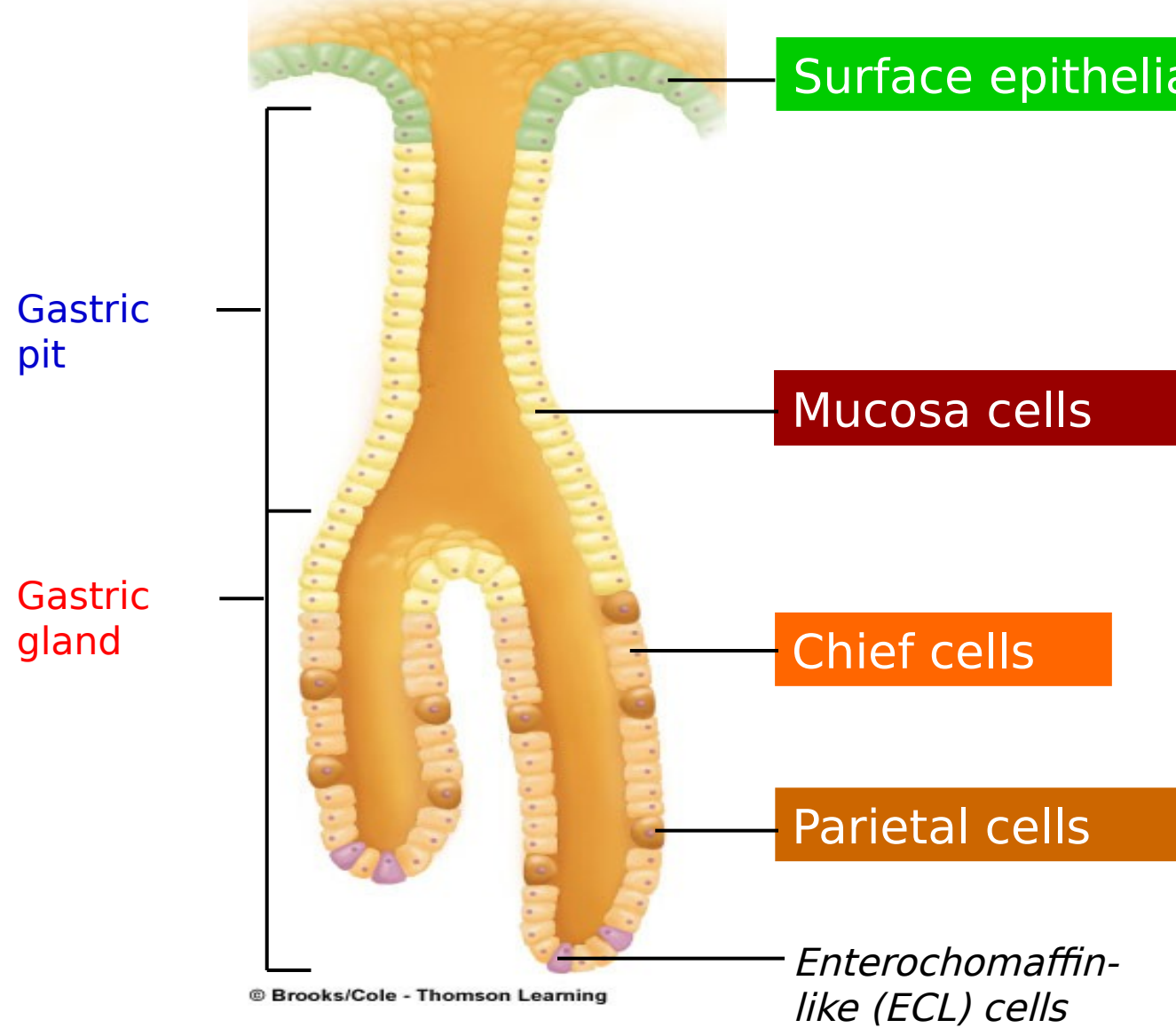
Site:

- Antrum

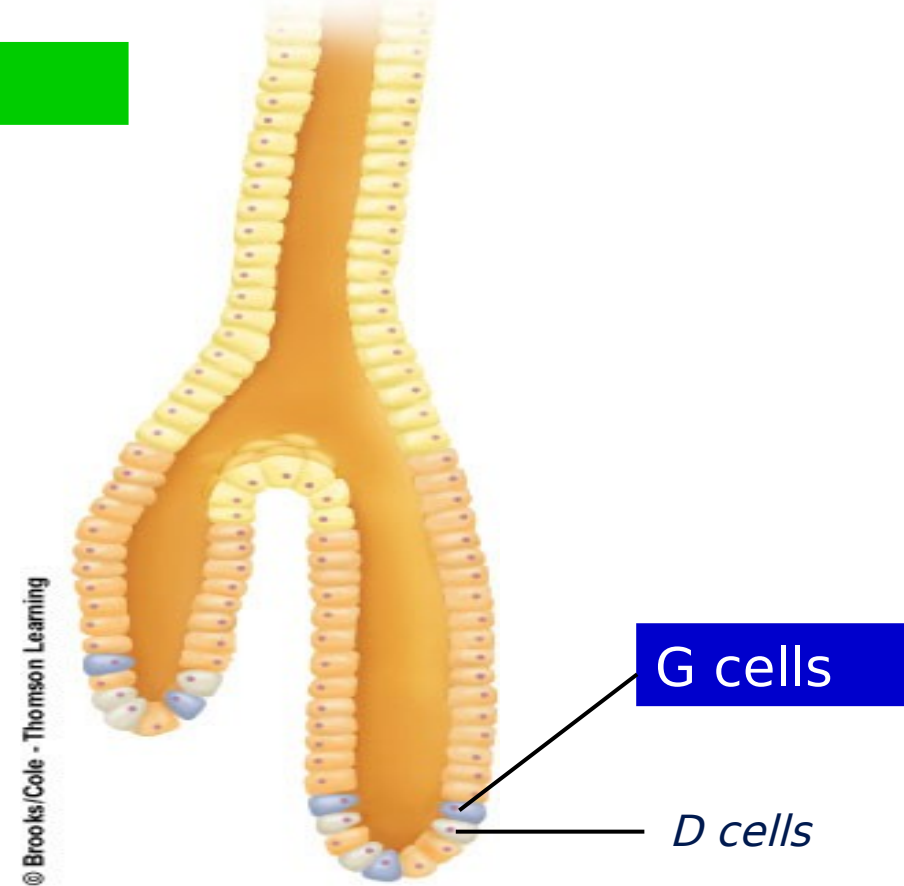
Contains

- D cells □ somatostatin.
- G cells □ gastrin.

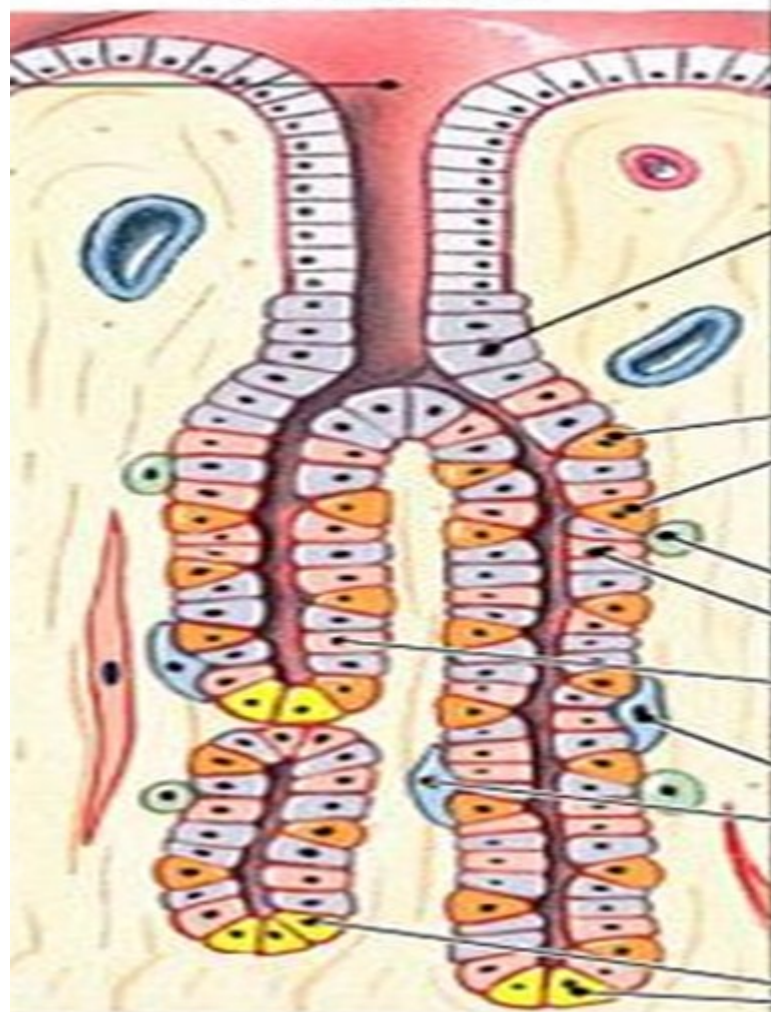
In oxyntic mucosa



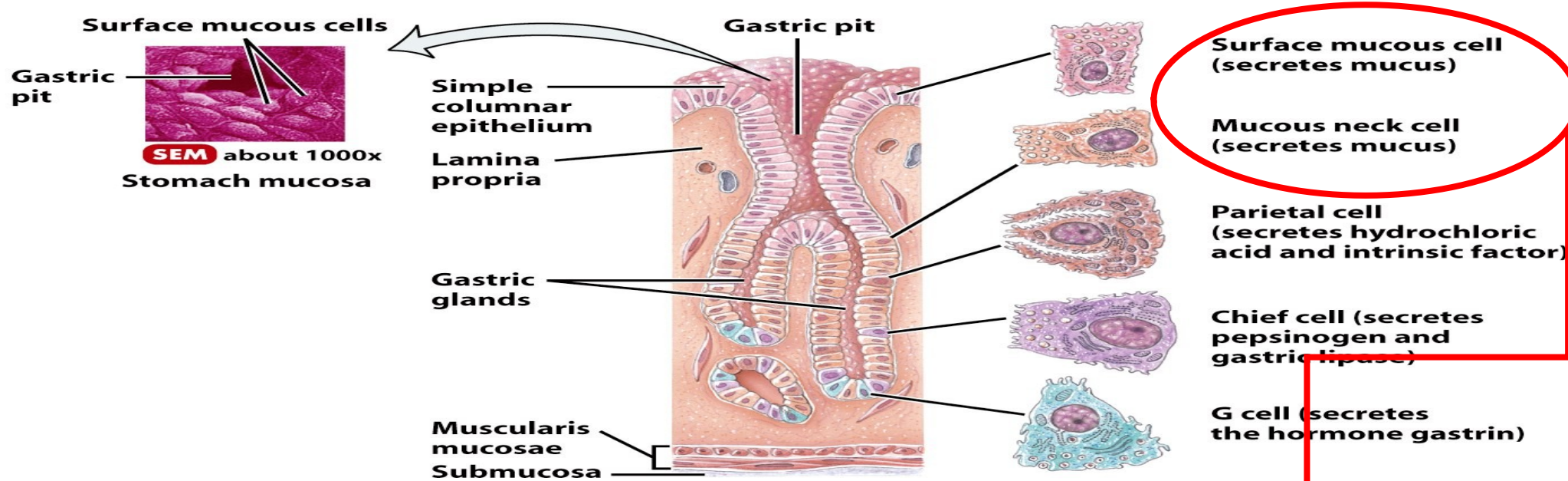
In pyloric gland area



Lumen of stomach



Cell Types	Substance Secreted
Mucous neck cell	Mucus (protects lining)
	Bicarbonate
Parietal cells	Gastric acid (HCl)
	Intrinsic factor
Enterochromaffin-like cell	Histamine (stimulates acid)
Chief cells	Pepsin(ogen)
	Gastric lipase
D cells	Somatostatin (inhibits acid)
G cells	Gastrin (stimulates acid)



Sectional view of the stomach mucosa showing gastric glands and cell types

Figure 23-11b Anatomy and Physiology: From Science to Life
© 2006 John Wiley & Sons

N.B:

- The surface epithelial cells of gastric mucosa secrete **thick alkaline viscid mucous** coat of mucosa protecting it from damage by the acid chyme. **Insoluble m**
- This mucous differ from the **thin watery mucous** secreted by the neck cells which & pepsin. It lubricates the gastric chyme. **Soluble mucous**

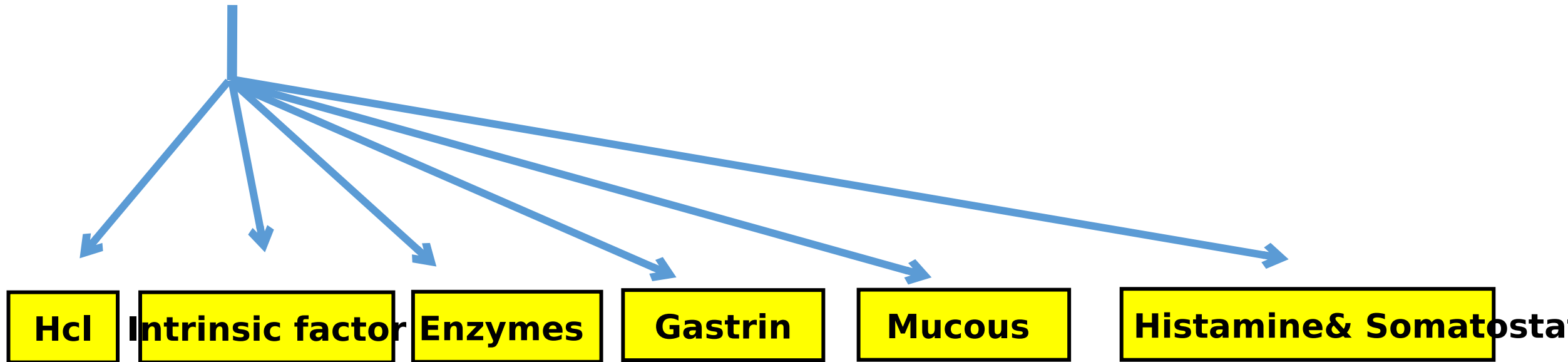
Functions of Stomach



Secretory function
(Gastric Mucosa)

Motor function

Storage function



Gastric juice :

- Volume: average 2.5 L/day.
- pH: 1 – 3.5, average 2

- **Contains:** Water, **HCl**, **intrinsic factor**, **pepsin**, **lipase** & **mucus** & small amounts of KCl and NaCl.

Gastric Secretion



Composition & Functions of Gastric Juice

Intrinsic factor

- Essential for absorption of vit B12 in terminal ileum

Mucous

- Protection against autodigestion & acid injury.

Histamine & Somatostatin

- Histamine $\square$ (+) parietal cells
- Somatostatin $\square$ (-) all cells

Enzymes

Gastrin

HCl

- **Pepsinogen** $\square$ pepsin
(proteolytic enzyme starts protein digestion)
Optimum pH 1-3.5

-Functions of HCl:

1. Activation of pepsinogen $\square$ pepsin
2. Provides optimum pH for action of pepsin.
3. Sterilization (*kill most of ingested microorganisms*)
3. Helps iron absorption.
4. Helps Ca^{++} absorption.

-Functions of gastrin:

1. (+) parietal cells $\square$ HCl.
2. (+) Chief cells $\square$ pepsinogen.
3. (+) ECL cells $\square$ histamine $\square$ + HCl.
4. Trophic effect.

Gastric Secretion



Gastric Mucosa

Surface Mucous Cell

Mucous

Parietal Cell

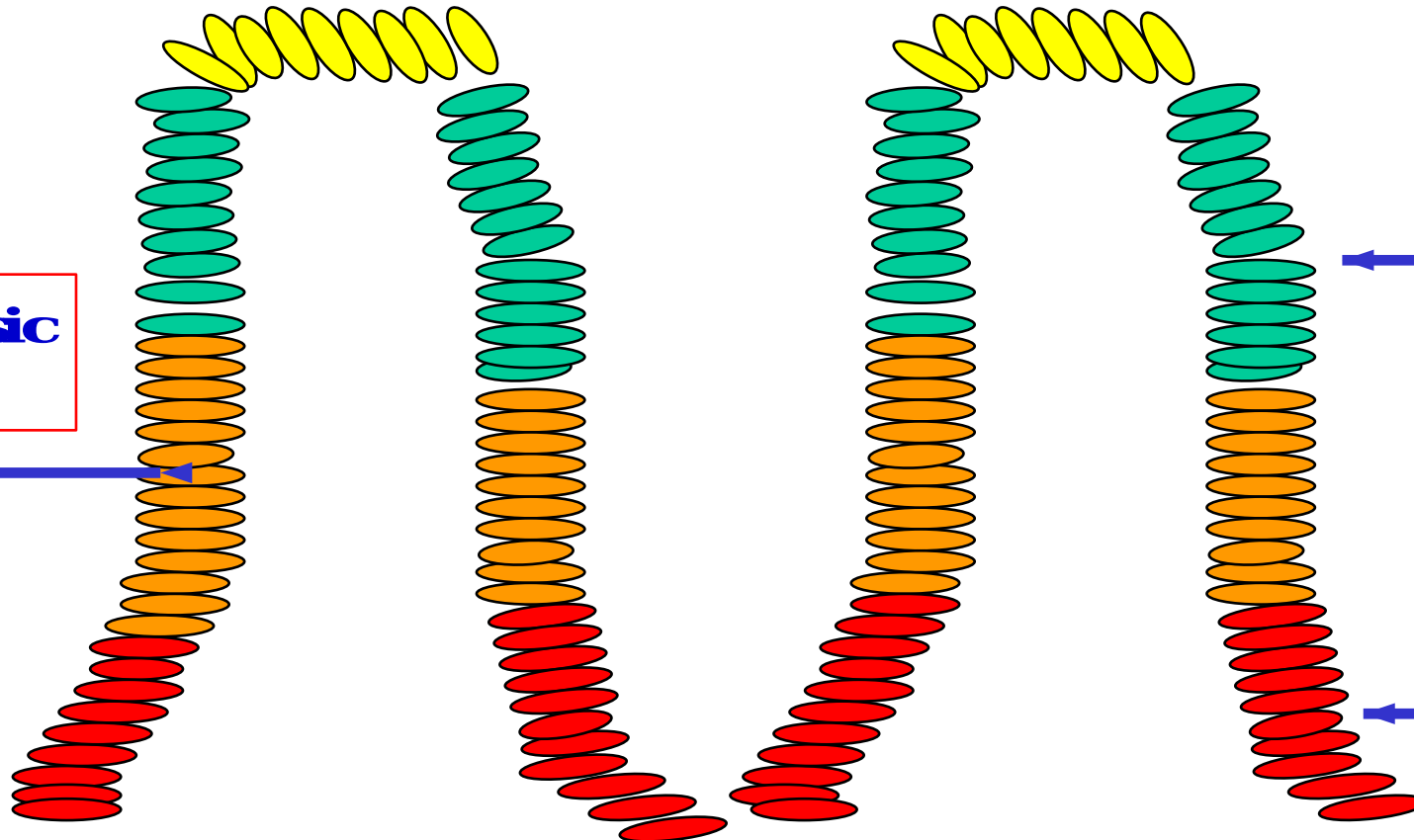
**HCl , Intrinsic
Factor**

Mucous Neck Cell

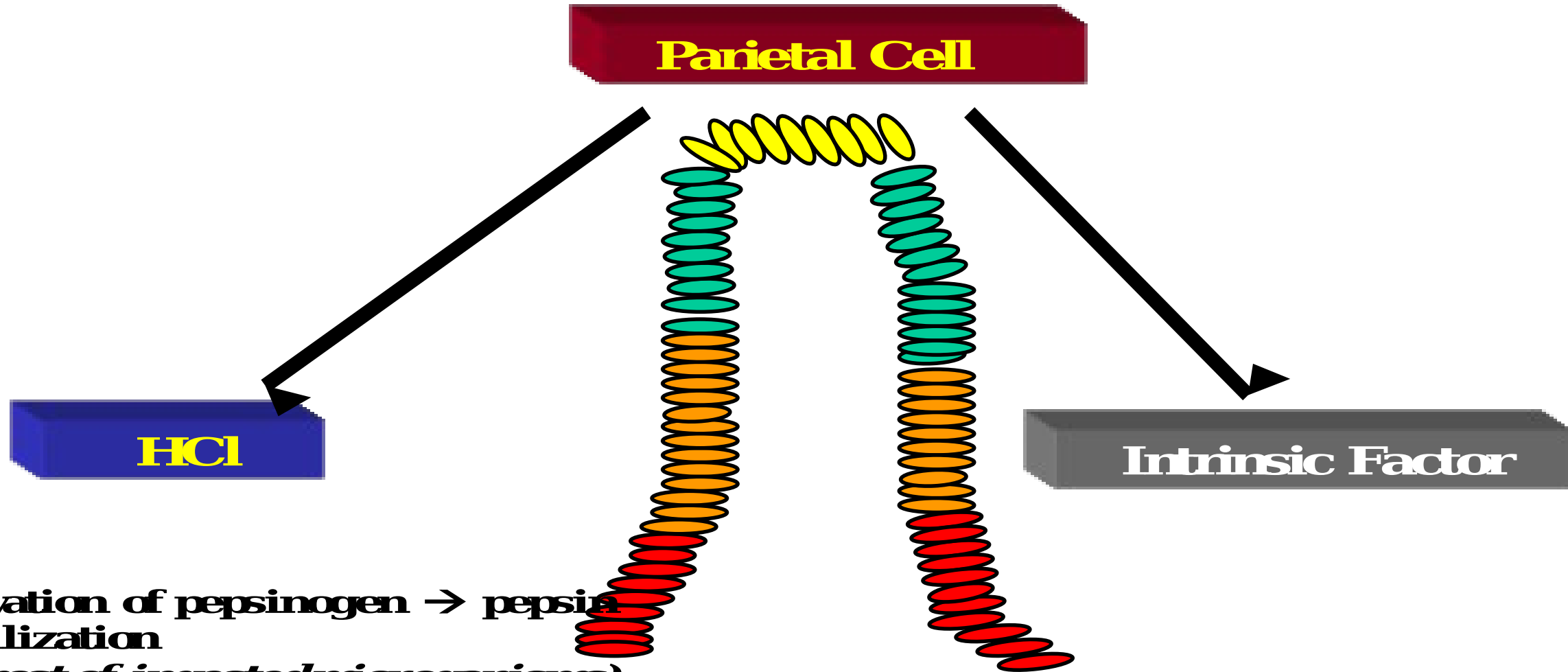
Mucous

Chief Cell

Pepsinogen



Gastric Secretion



1. Activation of pepsinogen $\rightarrow$ pepsin
2. Sterilization
(kill most of ingested microorganisms)
3. Help iron absorption.
4. Help Ca^{++} absorption.
5. Break down & dissolve food particles $\rightarrow$ chyme.

Gastric Secretion



Chief cell

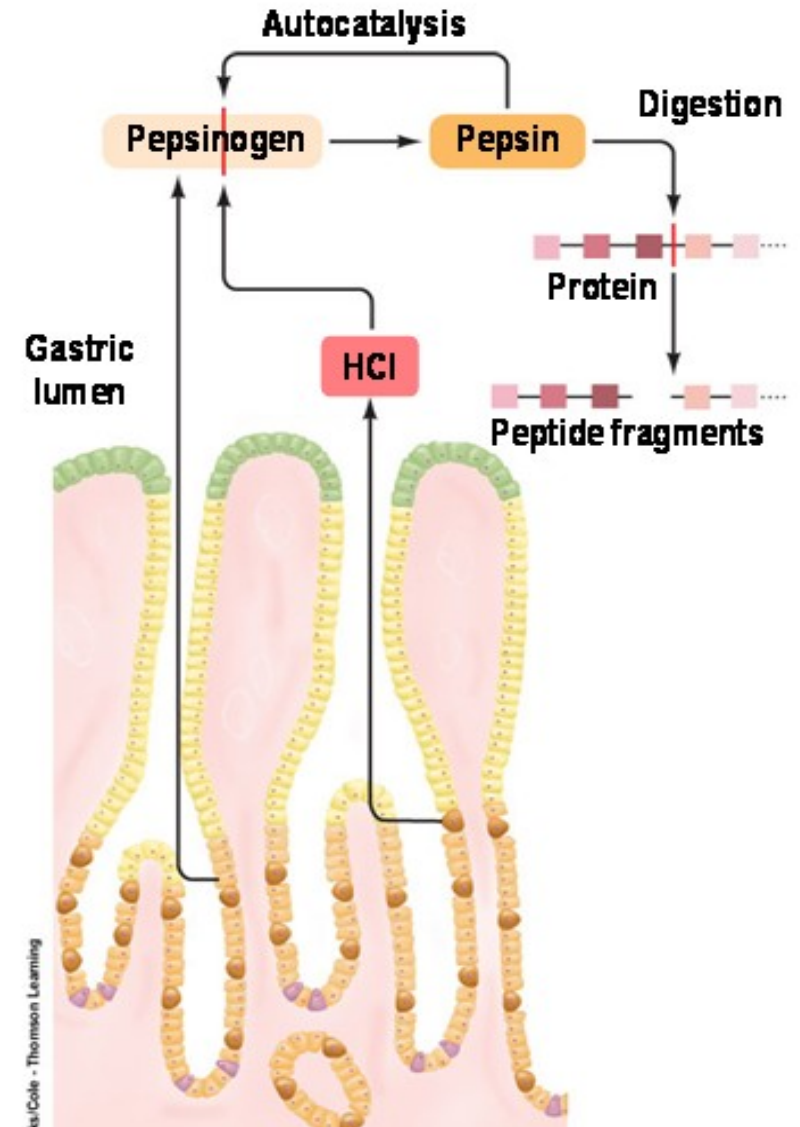


Pepsinogen is an inactive enzyme which is activated into pepsin by HCl in gastric lumen (*so that it does not digest the cells in which it is formed*)

Pepsin is an active proteolytic enzyme starts protein digestion by splitting certain amino acid linkages in proteins to produce smaller peptides. This active pepsin further activates pepsinogen i.e. positive feedback mechanism.

- Optimum pH 2-3.5

- Therefore, HCl activates pepsinogen into



Mechanism of hydrochloric acid (HCl) secretion



At basolateral

Secondary active transport

Cl-HCO₃ exchanger

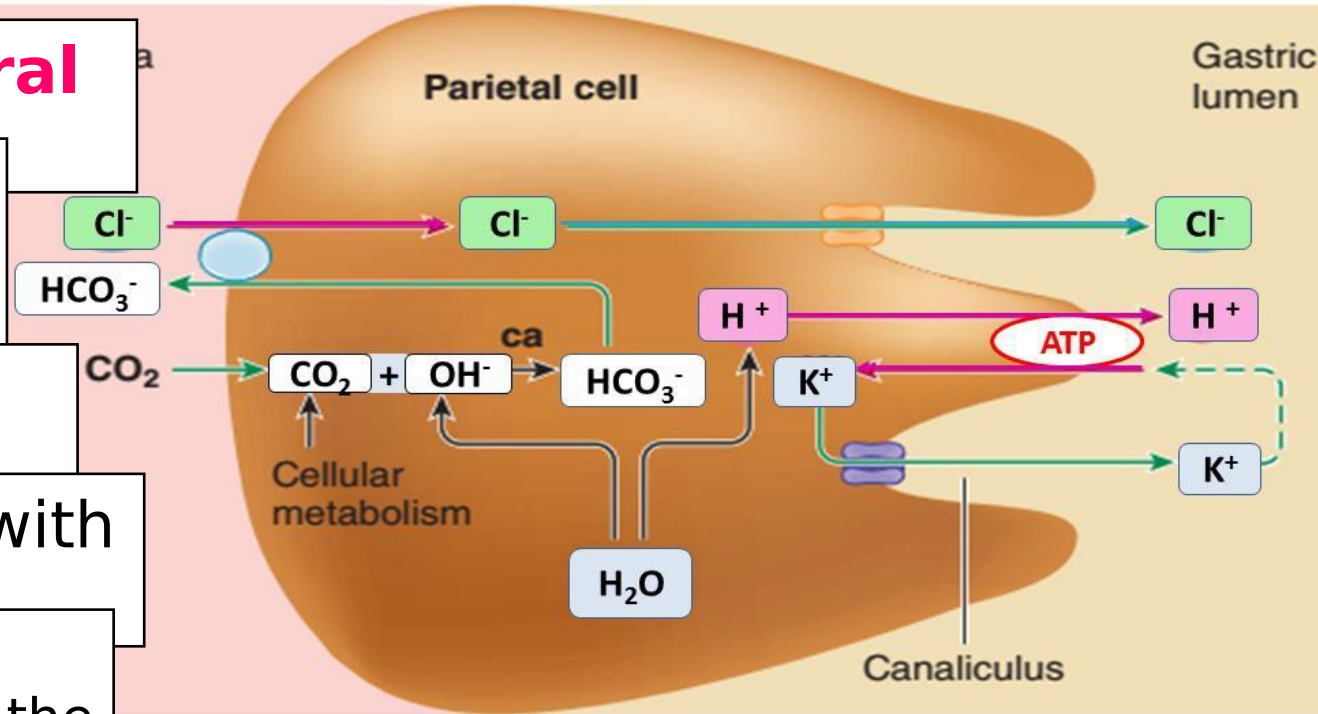
in exchange with

Cl⁻

Cl⁻ diffuse passively out of the cell through

luminal Cl⁻

The generated HCO₃⁻ comes from reaction of **CO₂** with OH⁻ in the presence of carbonic anhydrase enzyme.



→ = Active transport

→ = Secondary active transport

ca = Carbonic anhydrase

→ = Passive diffusion

→ = Chemical reaction

Mechanism of HCl secretion

At luminal

Primary active transport

H⁺/K⁺ATPase

in exchange with

K⁺

K⁺ passively leaks back into the lumen through luminal K⁺

Secreted H⁺ is derived from the breakdown of **water** into H⁺ and OH⁻

Mechanism of hydrochloric acid (HCl) secretion



- H^+ and Cl^- are actively secreted by 2 separate carriers in the parietal cell membrane:

1- Parietal cells pump H^+ into lumen in exchange with K^+ via an $H^+/K^+ATPase$ pump present at the luminal border.

(Primary active transport)

2- Cl^- is secreted by 2ry active transport in exchange with HCO_3^- , through $Cl^-HCO_3^-$ exchanger in the basolateral border then diffuses through a luminal Cl^- channel into the lumen.

(Secondary active transport)

Q. What is postprandial alkaline tide ?????

The blood leaving the stomach (gastric venous blood) is

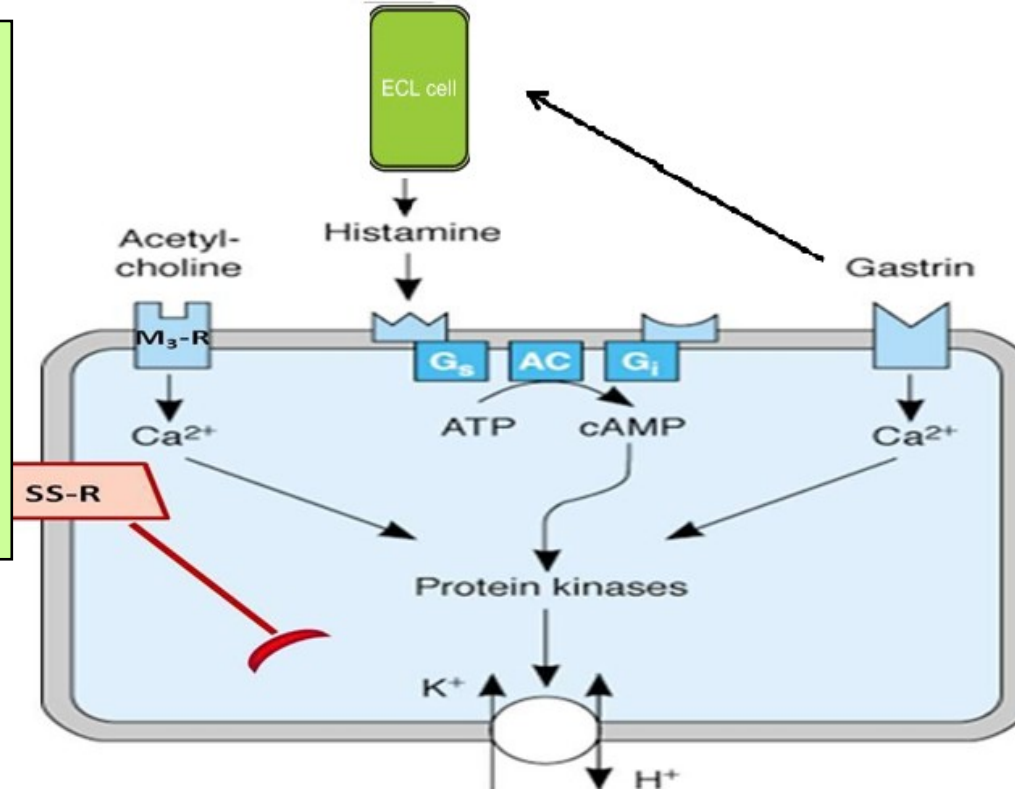
Regulation of acid secretion (HCL) by the parietal cell

(Stimulatory factors)



Acetylcholine (Ach)

-Acts on **M3** receptors $\rightarrow$ $\uparrow$ intracellular **Ca²⁺**.



Histamine

- Acts locally (paracrine) via **H₂** receptors $\rightarrow$ $\uparrow$ **cAMP**.

Gastrin

-Acts indirectly by (+) of ECL cells $\rightarrow$ $\uparrow$ **cAMP**.
{ main }
-Acts directly on **gastrin** receptors $\rightarrow$ $\uparrow$ **Ca²⁺**.

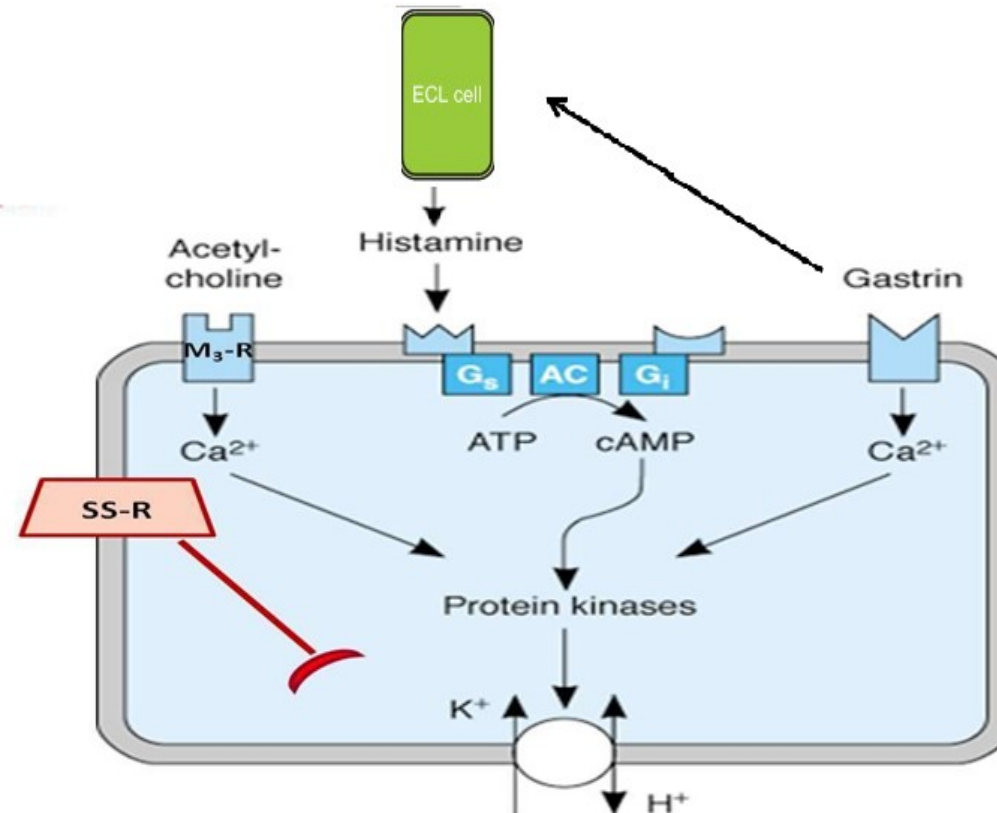
Regulation of acid secretion (HCL) by the parietal cell

(Inhibitory Factors)



Somatostatin

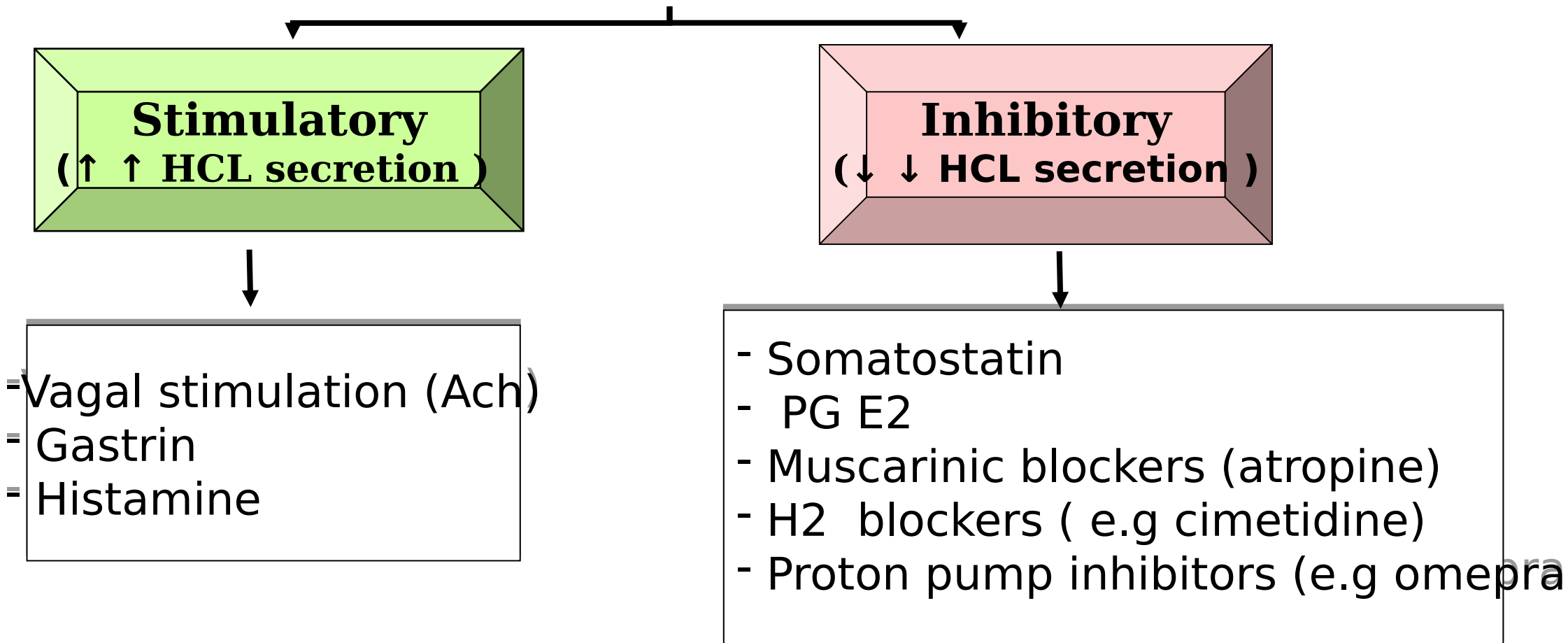
- Acts locally (paracrine)
- ↓ cAMP
- ↓ HCl secretion



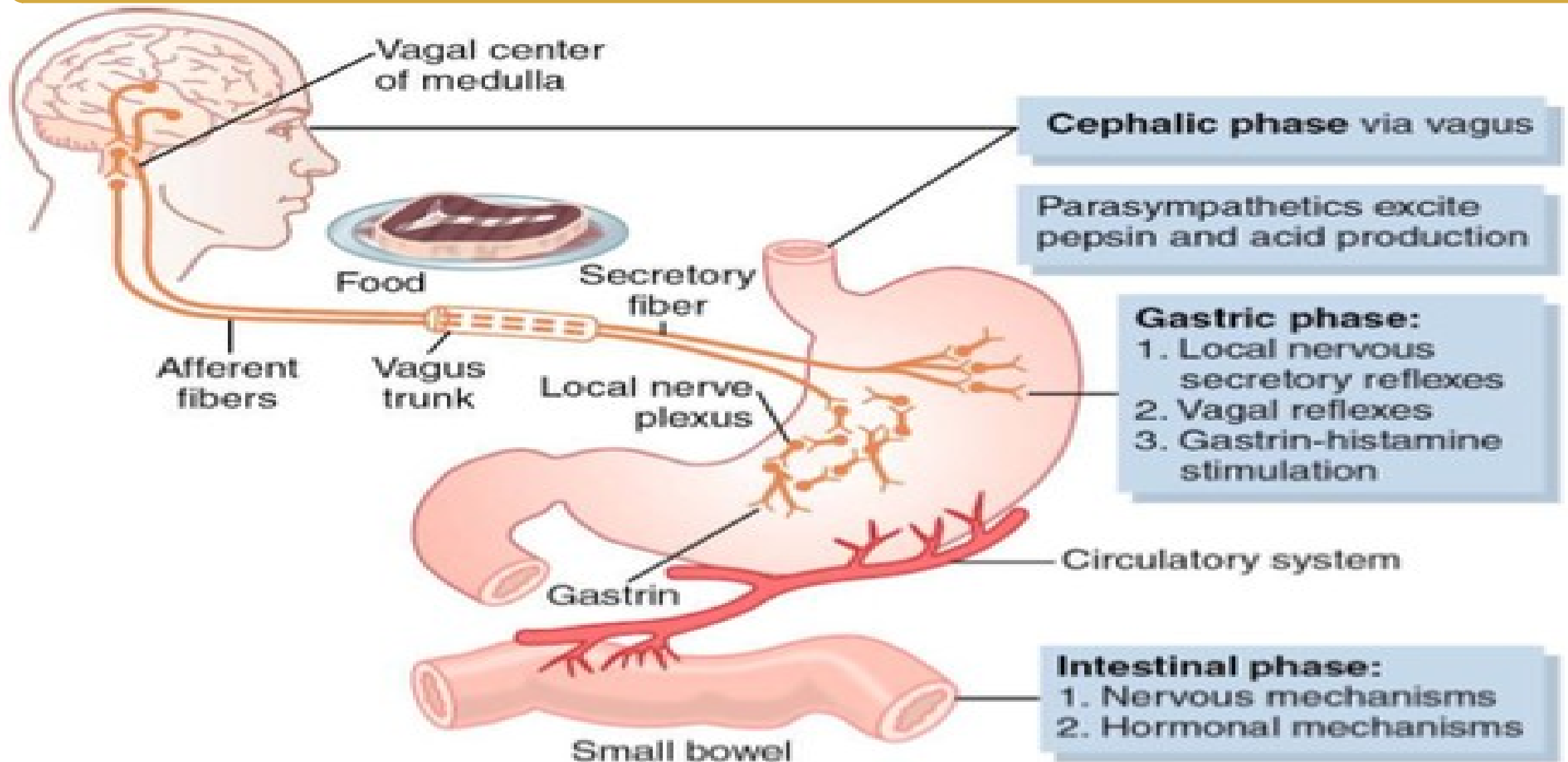
PG E₂

- Acts locally (paracrine)
- ↓ cAMP
- ↓ HCl secretion

Factors regulating HCL by parietal cells



Phases of Gastric Secretion



Phases of Gastric Secretion



Gastric secretion is divided into 3 phases:

Cephalic Phase

- ✓ Occurs before food enters stomach.
- ✓ Accounts for **20-25%** of the total gastric secretion.
- ✓ **Neural** mechanism.
- ✓ Stimulatory.

Gastric Phase

- ✓ Occurs when food actually reaches the stomach.
- ✓ Accounts for **70%** of the total gastric secretion.
- ✓ Both **neural** & **hormonal** mechanisms.

Intestinal Phase

- ✓ Occurs when food reaches the S. intestine (duodenum).
- ✓ Accounts for **5-10%** of the total gastric secretion.
- ✓ Both **neural** & **hormonal** mechanisms.
- ✓ Inhibitory (major role)

Control of gastric secretion



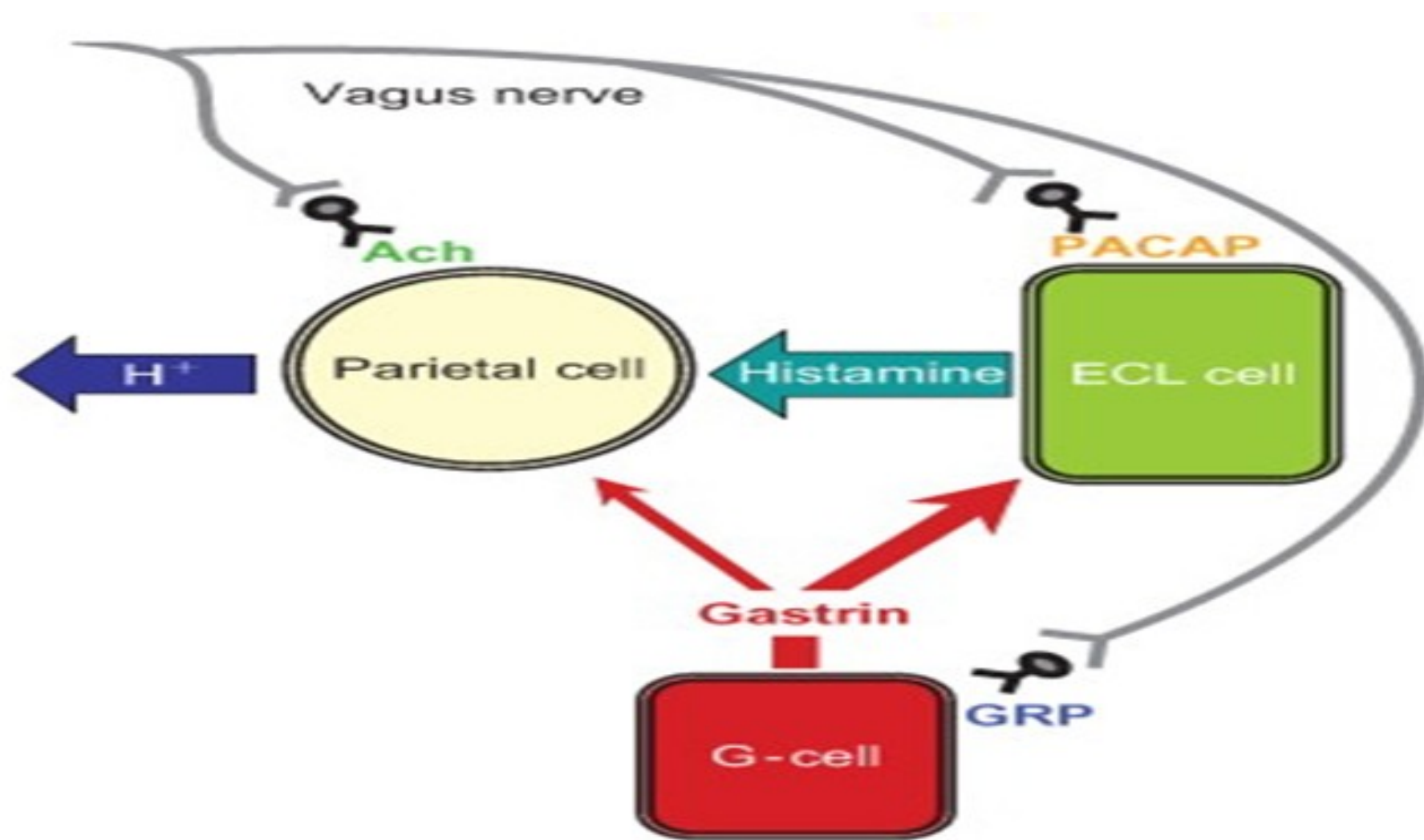
1. The cephalic stimulatory phase: (Nervous)

- Mechanism:

- Conditioned and unconditioned reflexes stimulate the dorsal nucleus of the vagus to increase secretions of HCl, pepsinogen, mucus and gastrin.
- The efferent fibers for this reflex are in the vagus nerves.

- Vagal stimulation increases gastric secretion by:

1. **Acetylcholine:** which acts directly on parietal & chief cells in fundus & body.
2. **Gastrin:** vagal nerve endings release gastrin-releasing peptide (GRP) that increases gastrin secretion from G cells in pyloric gland area.



Cephalic Phase

Conditioned reflexes

Seeing, smelling, hearing or thinking of food



Special senses



Cerebral cortex

Unconditioned reflexes

Presence of food in mouth e.g chewing, tasting, or swallowing of food



Tongue (taste receptors)

Vagal nucleus



Vagus nerve



Stomach

+++ Gastric secretion

Conditioned reflexes

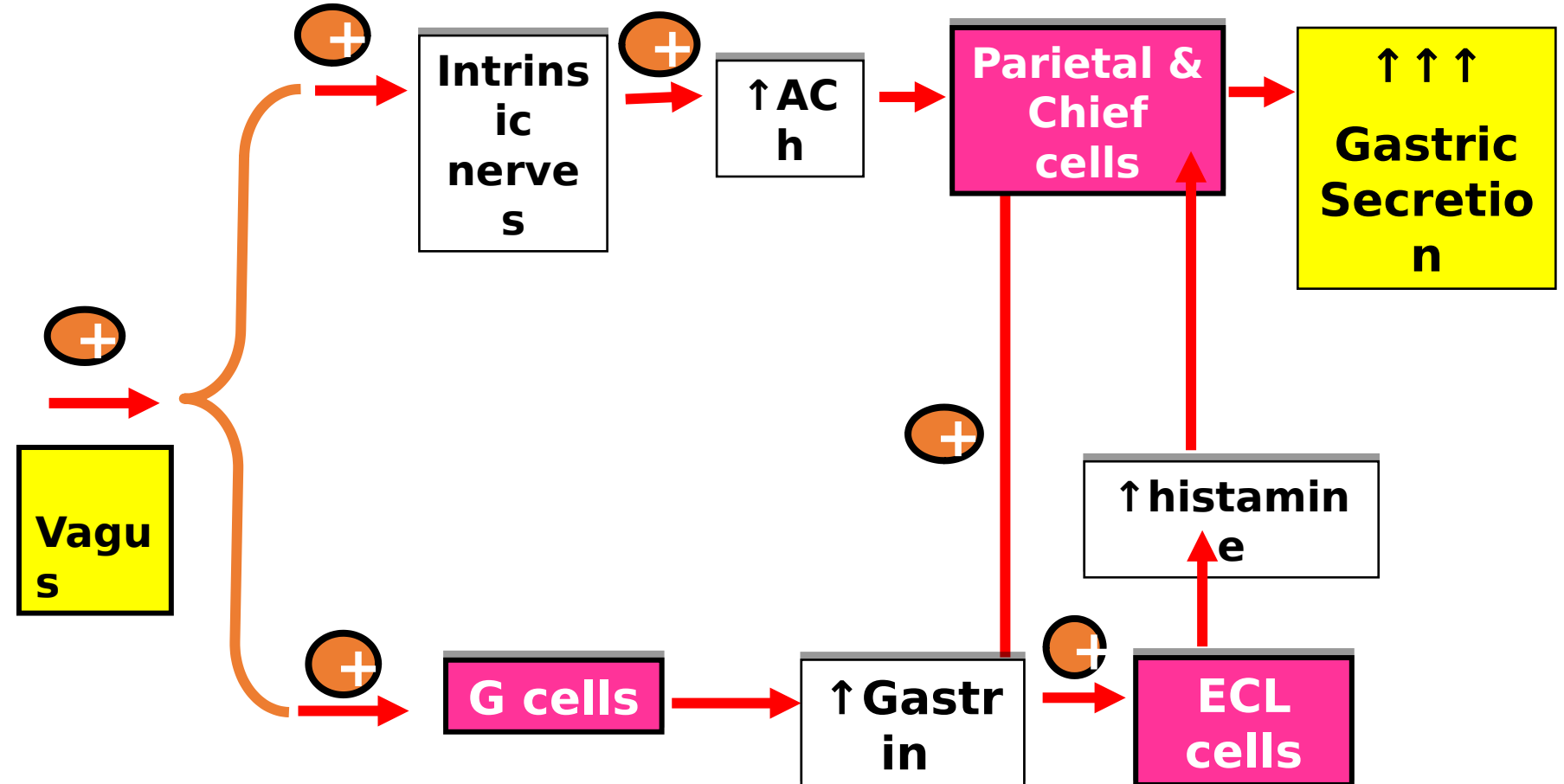
- 1- depend on the presence of cerebral cortex
- 2- are learned & established early in life

Both conditioned & unconditioned reflexes depend on the integrity of vagi so can be abolished by vagotomy or atropine injection

Cephalic Phase

Stimuli in the Head:

- Smelling, seeing, hearing or thinking of food
- Chewing, swallowing



Control of gastric secretion



2. The gastric stimulatory phase: (Nervous and Hormonal)

Mechanism:

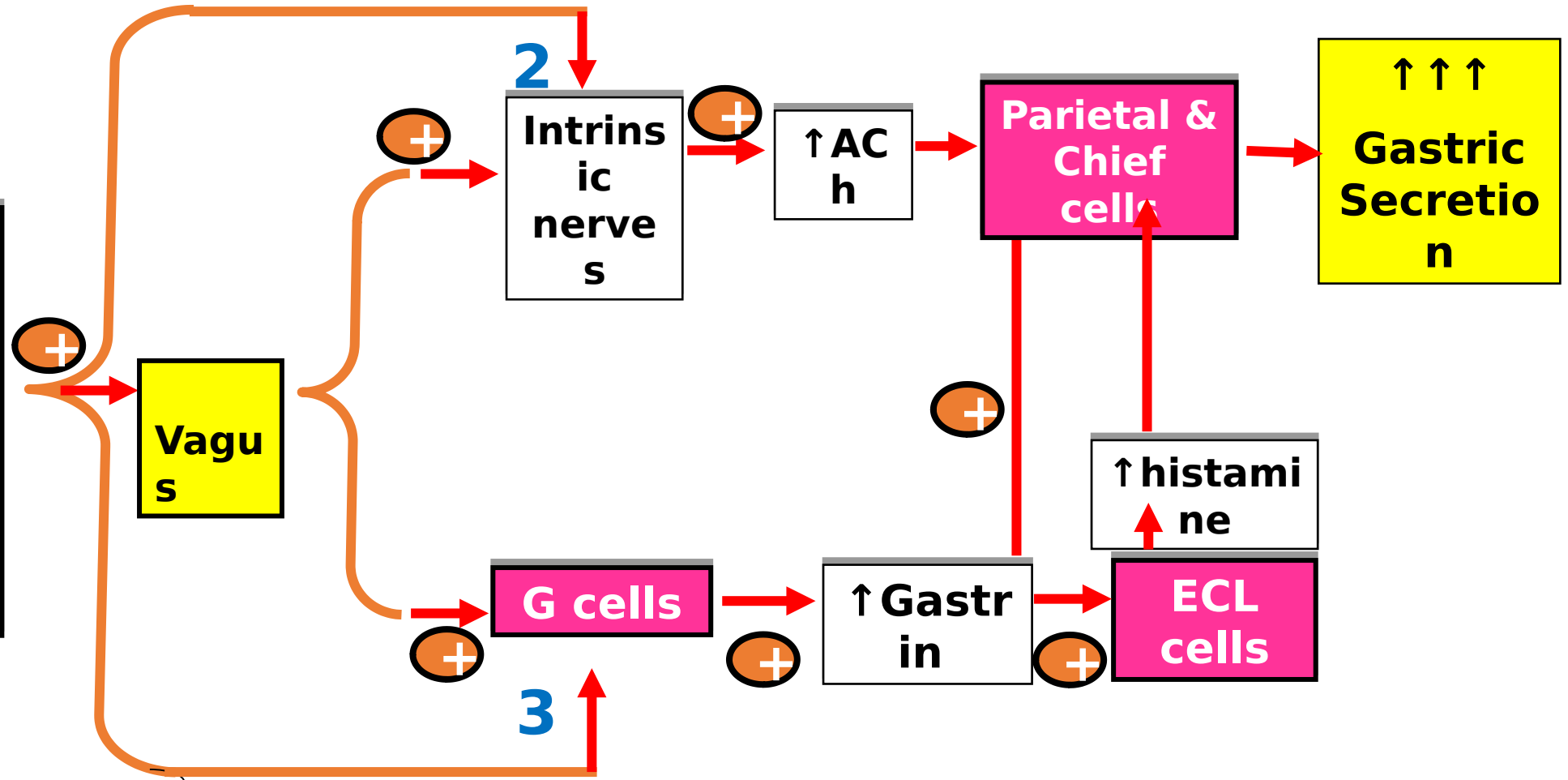
Presence of food in the stomach stimulates:

1. Long vagovagal reflexes like in cephalic phase.
2. Local enteric reflexes(enteric nervous system): Receptors in the wall of the stomach and the mucosa respond to stretch and chemical stimuli (mainly amino acids and related products of digestion). The sensory afferent fibres from the receptors enter the submucous plexus then efferent neurons end on parietal cells and stimulate acid secretion.
3. Gastrin secretion

Gastric Phase

Stimuli in stomach:

- Protein
- Distension
- Caffeine
- Alcohol



Control of gastric secretion



3. The intestinal inhibitory : (Nervous and Hormonal):

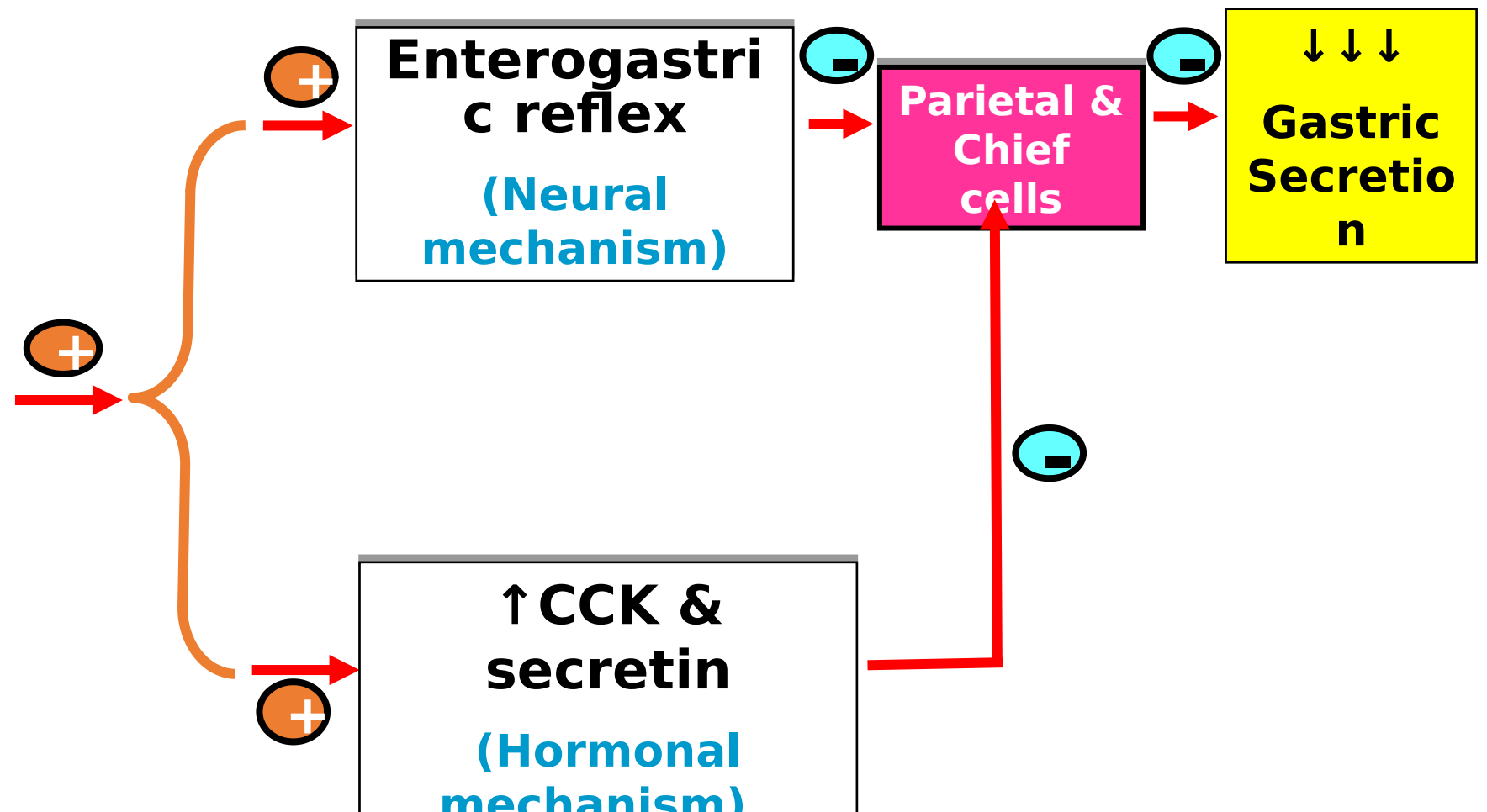
Mechanism:

- Presence of food in the duodenum inhibits gastric secretion by:
 1. Enterogastric reflex: which occurs due to presence of acid, fat content, hypertonic solutions, or distension of duodenum.
 2. Hormones: which inhibit gastric secretion, such as GIF, VIP, CCK and secretin.
 3. Emotional: depression and fear, via impulses from cerebral cortex, inhibit the dorsal vagal nucleus.

Intestinal Phase

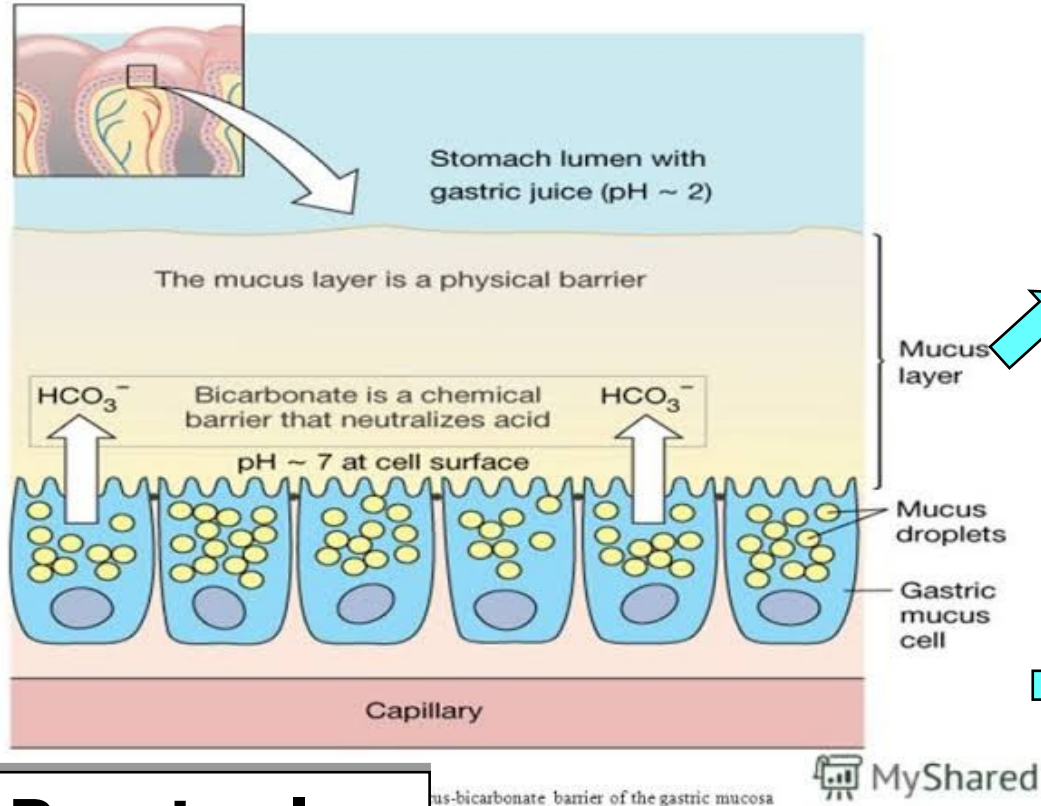
Stimuli in duodenum:

- Fat
- Acid
- Hypertonicity
- Distension



Protection of Gastric Mucosa

- The stomach is protected from acid injury and autodigestion by its proteolytic enzymes, because of the **gastric mucosal barrier** which includes



The **mucous** protective barrier

Thick, viscous, alkaline mucus to protect against:

1. Autodigestion by inhibiting pepsin.
2. Acid injury by neutralizing HCl.
3. Mechanical injury by lubricating food.

The **mucosal cell** barrier

Apical membranes of

mucosal cells are impermeable to H^+ .

2. Lateral edges of mucosal cells are joined together by tight junctions from the

The **rapid turnover** of the **mucosal cells**

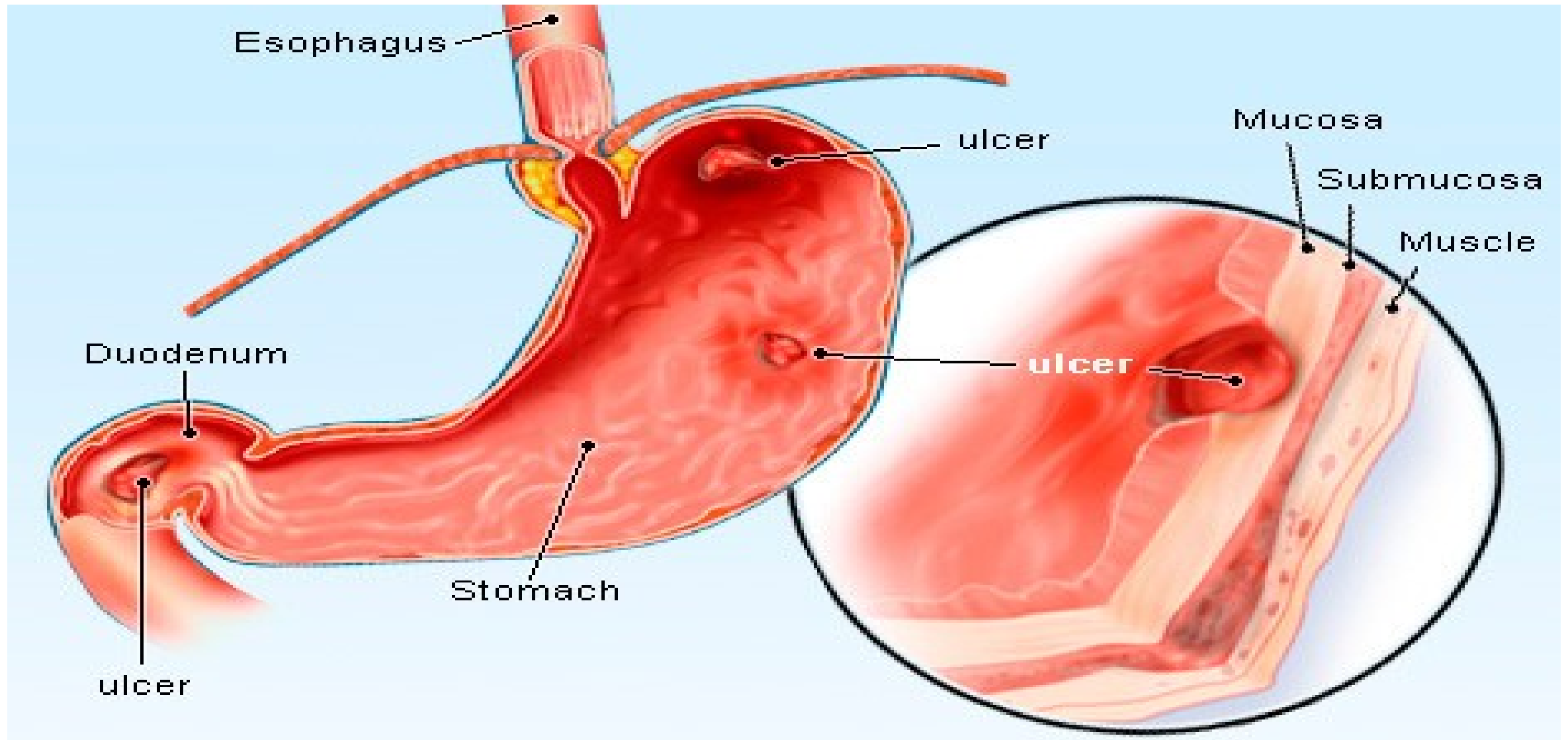
Continuous regeneration every 3 days

Prostaglandins

Released from mucosal cells:
secretion.

1. $\downarrow$ HCl.
2. $\uparrow$ mucus

Peptic ulcer



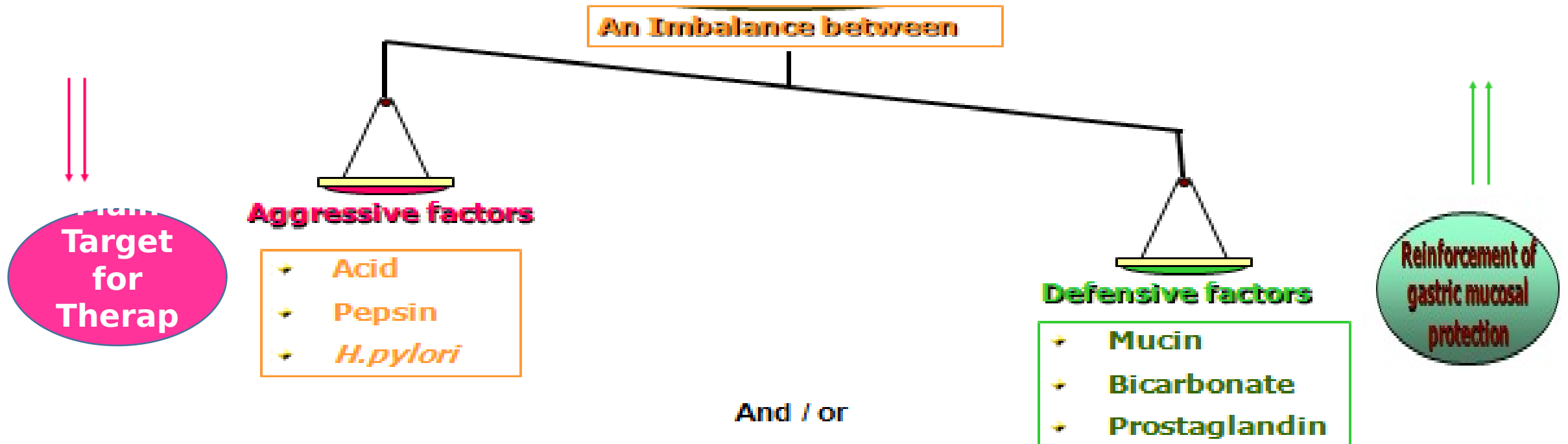
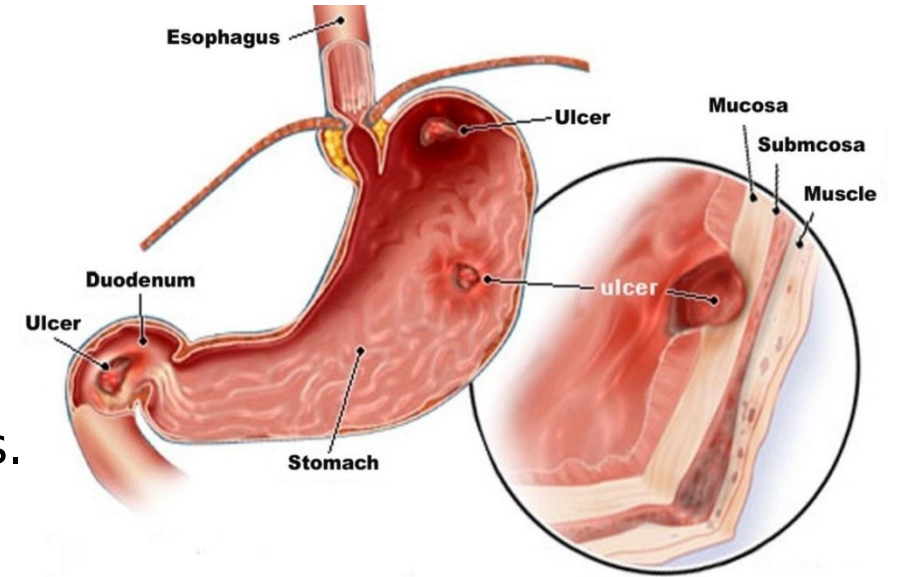
Peptic Ulcer

- Def:

An injured/eroded area in mucosa caused the action of gastric juice.

- Causes:

1. Excess secretion of HCL& pepsin e.g stress, gastrinomas.
2. Breakdown of gastric mucosal barrier e.g H.pylori, NSAIDs, alcohol & caffeine



Peptic ulcer



1. Breakdown of the gastric mucosal barrier :

Alcohol

Aspirin, and non-steroidal anti-inflammatory drugs; both inhibit the production of prostaglandins and consequently decrease mucus and HCO₃⁻ secretion.

Infection with specific bacteria called *Helicobacter pylori* which disrupts the mucosal barrier.



. Excess secretion of HCl:

Zollinger-Ellison syndrome, there is excess secretion of gastrin hormone by tumors in the pancreas. Gastrin causes prolonged secretion of acid and severe ulcers.

Lecture Quiz



Which of the following is secreted by stimulation of the parietal cell?

- a. HCl and intrinsic factor.
- b. HCl and pepsinogen.
- c. HCl and HCO_3^- .
- d. HCO_3^- and intrinsic factor.
- e. Mucus and pepsinogen.

Lecture Quiz



A patient with duodenal ulcer is treated with cimetidine, a drug that inhibits H^+ secretion by parietal cells. Which of the following is the mechanism of cimetidine action?

- a. Block muscarinic receptors.
- b. Stimulation of muscarinic receptors.
- c. Blocks $H-K^+$ ATPase.
- d. Decreased level of cAMP.
- e. Inhibition of somatoostatin.

Lecture Quiz



A 44 -year - old woman is diagnosed with Zollinger-Ellison syndrome. Which of the following findings is consistent with the diagnosis?

- a. Decreased serum gastrin levels.
- b. Increased insulin serum level.
- c. Decreased parietal cell mass.
- d. Peptic ulcer disease.
- e. Increased absorption of dietary lipids.

SUGGESTED TEXTBOOKS



1. Guton and Hall 11th edition, from page 795 to 799.
2. Ganong's 25th edition, from page 457 to 460.
3. Linda & Costanza 6th edition, from page 360 to 366.



Thank you